WHAT IS CLAIMED IS

1. A method of modulating a biological function of an endothelial cell or hematopoietic cell, comprising introducing into the cell an agent that inhibits binding of a PDZ protein and a PL protein in the cell, thereby modulating the biological function.

2. The method of claim 1, wherein the PL is selected from the group consisting of CD105, VCAM1, CD95, Spectrin β, KV1.3, DNAM1, Neuroligin 3, , CD44, CD38, CD3η, LPAP, CD46, CDw128B, DOCK2, PAG, CD34, and BLR-1.

3. The method of claim 2, wherein the PDZ is selected from the group consisting of MPP1, K303, K807, DLG1, PSD95, NeDLG, IP43, LDP, LIM, K545, TIP1, PTN-4, CBP, AF6, PDZK1, DLG5, Syntenin, WWP3, and K561.

4. The method of claim 1, wherein

a) the PDZ protein is MPP1 and the PL protein has a carboxy-terminal amino acid motif X-S/T/Y/I-X-V;

b) the PDZ protein is LIMK1 and the PL protein has a carboxy-terminal amino acid motif X-S/T/Y-X-V;

c) the PDZ protein is K303 and the PL protein has a carboxy-terminal amino acid motif X-S-X-V;

d) the PDZ protein is K807 and the PL protein has a carboxy-terminal amino acid motif X1-S/T-X2-V/I/L/F;

e) the PDZ protein is DLG1, PSD95, or NeDLG and the PL protein has a carboxy-terminal amino acid motif X-S/T/Y/A/E-X-V/I/L;

f) the PDZ protein is SNTa1 and the PL protein has a carboxy-terminal amino acid motif X-S/T/Y-D/Y-V/I/L;

g) the PDZ protein is DVL1 and the PL protein has a carboxy-terminal amino acid motif X-S/T/Y-X-V;

h) the PDZ protein is LDP and the PL protein has a carboxy-terminal amino acid motif X-A/S-X2-V/I;

i) the PDZ protein is LIM and the PL protein has a carboxy-terminal amino acid motif X-S/T-X2-A/V;

j) the PDZ protein is K561 and the PL protein has a carboxy-terminal amino acid motif X-S/T/Y-X-V/I/L/F;

k) the PDZ protein is K545 and the PL protein has a carboxy-terminal amino acid motif X-A/S/T/Y-M-A/S/V;

l) the PDZ protein is TAX-IP2 and the PL protein has a carboxy-terminal amino acid motif X-S-D/E-V;

m) the PDZ protein is MPP2 and the PL protein has a carboxy-terminal amino acid motif X-S/T/Y-X-A/V/I;

n) the PDZ protein is TIP-1 and the PL protein has a carboxy-terminal amino acid motif X-S/T-X2-V/I/L;

o) the PDZ protein is PTN-4 and the PL protein has a carboxy-terminal amino acid motif X1-S/T-X-V/F;

p) the PDZ protein is prIL16 and the PL protein has a carboxy-terminal amino acid motif D/E/K/R-V/I/L/F/Y-X-V;

q) the PDZ protein is CBP and the PL protein has a carboxy-terminal amino acid motif X-S/T-F/Y-V;

r) the PDZ protein is protein 41 and the PL protein has a carboxy-terminal amino acid motif X-A/S/T/Y/F-X-A/V/I/L;

s) the PDZ protein is AF6 and the PL protein has a carboxy-terminal amino acid motif X-A/S/T/Y-F/Y-V/I/L;

t) the PDZ protein is RGS12 and the PL protein has a carboxy-terminal amino acid motif X1-S/T/Y-X-V/F;

v) the PDZ protein is PDZK1 and the PL protein has a carboxy-terminal amino acid motif X-T-X-F;

w) the PDZ protein is DLG5 and the PL protein has a carboxy-terminal amino acid motif X-S/T-X-V;

x) the PDZ protein is Synt and the PL protein has a carboxy-terminal amino acid motif X1-V/I/L-X2-V;

y) the PDZ protein is WWP3 and the PL protein has a carboxy-terminal amino acid motif X-S/T-X2-V; and,

z) the PDZ protein is TAX-IP40 and the PL protein has a carboxy-terminal amino acid motif X-Y-X-V;

where X is any amino acid, X1 is any amino acid, X2 is any amino acid.

5. The method of claim 2 wherein the agent is a peptide comprising a sequence of at least the carboxy-terminal two residues of the PL protein.

6. The method of claim 4 wherein the agent is a peptide comprising a sequence of at least the carboxy-terminal three residues of the PL protein.

7. The method of claim 2 wherein the agent is a small molecule or peptide mimetic of the carboxy-terminus of the PL protein.

8. The method of claim 4, wherein the cell is a T cell or a B cell.

9. A method of determining whether a test compound is an inhibitor of binding between a PDZ protein and a PL protein comprising:

a) contacting

i) a PDZ domain polypeptide having a sequence from the PDZ protein, and

ii) a PL peptide, wherein the PL peptide comprises a C-terminal sequence of a PL protein selected from the group consisting of CD105, VCAM1, CD95, Spectrin β, KV1.3, DNAM1, Neuroligin 3, TAX, CD44, CD38, CD3η, LPAP, CD46, CDw128B, DOCK2, PAG, CD34, and BLR-1 under conditions in which they form a complex

wherein said contacting is carried out in the presence and in the absence of a test compound;

b) detecting the formation of the complex in the presence and absence of the test compound

wherein less complex formation in the presence of the test compound than in the absence of the compound indicates that the test compound is an inhibitor of a PDZ protein -PL protein binding.

10. An inhibitor identified by the method of claim 9.

11. The inhibitor of claim 9 that is

(a) a peptide comprising a sequence that is from 3 to about 20 residues of a C-terminal sequence of a PL protein selected from CD105, VCAM1, CD95, Spectrin β, KV1.3, DNAM1, Neuroligin 3, TAX, CD44, CD38, CD3η, LPAP, CD46, CDw128B, DOCK2, PAG, CD34, and BLR-1;

(b) a peptide mimetic of a peptide of section (a); or

(c) a small organic molecule with a molecular weight less than 1 kD.

12. A pharmaceutical composition comprising an inhibitor of claim 11.

13. A method for treating a disease characterized by leukocyte activation, comprising administering a therapeutically effective amount of an inhibitor of claim 11.

14. The method of claim 13 wherein the disease is characterized by an inflammatory or humoral immune response.

15. The method of claim 14 wherein the disease is an autoimmune disease.

16. A method of modulating a biological function of a cell, comprising introducing into the cell an antagonist that inhibits binding of a PDZ protein and a PL protein in the cell, wherein,

a) the PDZ protein is MPP1 (p55) and the PL is Spectrin β;

b) the PDZ protein is K303 and the PL is Spectrin β;

c) the PDZ protein is K807 and the PL VCAM1, Spectrin β, KV1.3, Neuroligin 3, CD38, CD3η, LPAP, CD46 (form 1), CDw128B, DOCK2, PAG, CD34, or BLR-1;

d) the PDZ protein is DLG1 and the PL is Spectrin;

e) the PDZ protein is PSD95 and the PL is Spectrin β, CD34, or CD38;

f) the PDZ protein is NeDLG and the PL is Spectrin β or CD38;

g) the PDZ protein is TAX IP43 and the PL is Spectrin β or CD38;

h) the PDZ protein is LDP and the PL is CD38;

i) the PDZ protein is LIM and the PL is CD105;

j) the PDZ protein is K545 and the PL is CD105;

k) the PDZ protein is TIP1 and the PL is CD95, KV1.3, CD3η, LPAP;

l) the PDZ protein is PTN-4 and the PL is Spectrin β;

m) the PDZ protein is CBP and the PL is Spectrin β;

n) the PDZ protein is AF6 and the PL is Spectrin β;

o) the PDZ protein is PDZK1 and the PL is BLR-1;

p) the PDZ protein is DLG5 and the PL is Spectrin;

q) the PDZ protein is Syntenin and the PL is CD44;

r) the PDZ protein is WWP3 and the PL is VCAM1, Spectrin β, DNAM1,

Neuroligin 3;

s) the PDZ protein is K561 and the PL is BLR-1.

17. The method of claim 16 wherein the cell is a hematopoietic cell.